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search clms 1-9, pls.
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heparinase

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STRUCTURE FILE UPDATES:  21 MAY 93   HIGHEST RN 147730-39-0
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=> e heparinase ii/cn 5
E1             1      HEPARINASE/CN
E2             1      HEPARINASE I/CN
E3             1 -->  HEPARINASE II/CN
E4             1      HEPARINASE III/CN
E5             1      HEPARINIC ACID/CN

=> s e2-e4
               1 "HEPARINASE I"/CN
               1 "HEPARINASE II"/CN
               1 "HEPARINASE III"/CN
L1             2 ("HEPARINASE I"/CN OR "HEPARINASE II"/CN OR "HEPARINASE II
                 I"/CN)

=> e heparin sulfate/cn 5
E1             1      HEPARIN SULFAMIDASE/CN
E2             1      HEPARIN SULFATASE/CN
E3             1 -->  HEPARIN SULFATE/CN
E4             1      HEPARIN SULFATE ELIMINASE/CN
E5             1      HEPARIN SULFATE ENDOGLYCOSIDASE/CN

=> s e3
L2             1 "HEPARIN SULFATE"/CN

=> e hydroxyapatite/cn 5
E1             1      HYDROXYANOPTERYL ALCOHOL/CN
E2             1      HYDROXYANTHRAQUINONE/CN
E3             1 -->  HYDROXYAPATITE/CN
E4             1      HYDROXYAPOPHYLLITE/CN
E5             1      HYDROXYAPOPHYLLITE (CA4KSI8((OH)0.5-1F0-0.5)020.8H2O)/
                      CN

=> s e3
L3             1 HYDROXYAPATITE/CN

=> s albumin/cn
L4             0 ALBUMIN/CN

=> fil ca
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abstract graphic structures.  The AB format DOES NOT display structure
diagrams.

=> s (l1 or l2 or l3 or (heparinase(w)(i or ii or iii))/ia)
           150 L1
          9543 L2
          3831 L3
           140 HEPARINASE/BI
           385 HEPARINASE/AB
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          407 HEPARINASE/IA
                (HEPARINASE/BI,AB)
       206899 I/BI
      1999442 I/AB
      2125075 I/IA
                (I/BI,AB)
       259479 II/BI
       816848 II/AB
       987007 II/IA
                (II/BI,AB)
       124266 III/BI
       358300 III/AB
       444398 III/IA
                (III/BI,AB)
           15 (HEPARINASE(W)(I OR II OR III))/IA
L5      13440 (L1 OR L2 OR L3 OR (HEPARINASE(W)(I OR II OR III))/IA)

=> s l5 and ((h or heparinum)(W)favobacteri?)/ia
        40486 H/BI
      1292196 H/AB
      1307913 H/IA
                (H/BI,AB)
           84 HEPARINUM/BI
          107 HEPARINUM/AB
          122 HEPARINUM/IA
                (HEPARINUM/BI,AB)
            1 FAVOBACTERI?/BI
            0 FAVOBACTERI?/AB
            1 FAVOBACTERI?/IA
                (FAVOBACTERI?/BI,AB)
            0 ((H OR HEPARINUM)(W)FAVOBACTERI?)/IA
L6          0 L5 AND ((H OR HEPARINUM)(W)FAVOBACTERI?)/IA

=> s l5 and ((h or heparinum)(W)flavobacteri?)/ia
        40486 H/BI
      1292196 H/AB
      1307913 H/IA
                (H/BI,AB)
           84 HEPARINUM/BI
          107 HEPARINUM/AB
          122 HEPARINUM/IA
                (HEPARINUM/BI,AB)
         1367 FLAVOBACTERI?/BI
         1193 FLAVOBACTERI?/AB
         1684 FLAVOBACTERI?/IA
                (FLAVOBACTERI?/BI,AB)
            0 ((H OR HEPARINUM)(W)FLAVOBACTERI?)/IA
L7          0 L5 AND ((H OR HEPARINUM)(W)FLAVOBACTERI?)/IA

=> s l5 and flavobacter?/ia
         1376 FLAVOBACTER?/BI
         1214 FLAVOBACTER?/AB
         1704 FLAVOBACTER?/IA
                (FLAVOBACTER?/BI,AB)
L8         91 L5 AND FLAVOBACTER?/IA

=> s l8 and (l2 or l3 or (heparin sulfate or hydroxyapatite)/ia)
         9543 L2
         3831 L3
        10596 HEPARIN/BI
        17052 HEPARIN/AB
        18502 HEPARIN/IA
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                    (HEPARIN/BI,AB)
        125912 SULFATE/BI
        120776 SULFATE/AB
        205515 SULFATE/IA
                    (SULFATE/BI,AB)
           374 HEPARIN SULFATE/IA
                    ((HEPARIN(W)SULFATE)/IA)
          2413 HYDROXYAPATITE/BI
          3954 HYDROXYAPATITE/AB
          4702 HYDROXYAPATITE/IA
                    (HYDROXYAPATITE/BI,AB)
L9          68 L8 AND (L2 OR L3 OR (HEPARIN SULFATE OR HYDROXYAPATITE)/IA
               )

=> s l9 and (protein or albumin)/ia
        366325 PROTEIN/BI
        470644 PROTEIN/AB
        594127 PROTEIN/IA
                    (PROTEIN/BI,AB)
         19551 ALBUMIN/BI
         52424 ALBUMIN/AB
         55386 ALBUMIN/IA
                    (ALBUMIN/BI,AB)
L10          7 L9 AND (PROTEIN OR ALBUMIN)/IA

=> d 1-7 .mh
```

L10 ANSWER 1 OF 7 COPYRIGHT 1993 ACS
TI Purification and characterization of a novel heparinase
SO J. Biol. Chem., 265(23), 13609-17
AU Bohmer, Linde H.; Pitout, Marthinus J.; Steyn, Pieter L.; Visser, Leon
PY 1990
AN CA113(17):147733b
AB A unique heparinase was isolated from a recently discovered Gram-neg. soil bacterium. The enzyme (heparinase III) was purified by hydroxylapatite chromatog., chromatofocusing, and gel permeation chromatog. The enrichment was 48-fold, and the specific activity of catalytically pure heparinase was 127 IU/mg of protein. Similar to the heparinase I from Flavobacterium heparinum, heparinase III also degrades heparin to mainly disaccharide fragments. It is specific for heparin and also breaks down heparan sulfate, but not hyaluronic acid and chondroitin sulfate. Heparinase III, however, differs markedly from heparinase I in several other aspects: it has a higher mol. mass (94 vs. 43 kDa) and pI (9.2 vs. 8.5), its Kcat are different, and it has a higher energy of activation (15.6 vs. 6.3 kcal/mol). Optimal activity was also at higher pH (7.6 vs. 6.5) and temp. (45 vs. 37.degree.). Furthermore, the amino acid compn. of heparinase III is quite different from that of heparinase I.

L10 ANSWER 2 OF 7 COPYRIGHT 1993 ACS
TI Interaction of platelet factor four with cultured vascular endothelial cells
SO Blood, 73(6), 1534-9
AU Rybak, Mary Ellen; Gimbrone, Michael A., Jr.; Davies, Peter F.; Handin, Robert I.
PY 1989
AN CA111(1):4908k
AB 125I-labeled platelet factor 4 (PF-4) was incubated with cell

suspensions derived from confluent monolayers of cultured bovine aortic endothelium. Binding of 125I-labeled PF-4 was inhibited by a 100-fold excess of nonradioactive PF-4 and varied with duration and temp. of incubation. At 4.degree., binding reached equil. at 20 min with a dissocn. const. (kd) = 2.87 .mu.M and max. binding capacity (Bmax) of 63.83 pmol/105 cells. Binding capacity was reduced 83.4% by brief incubation of endothelial cells with trypsin and 46.67% by incubation with Flavobacterium heparinase, but was unchanged by chrondroitin-ABCase treatment. At 37.degree., PF-4 was internalized by confluent monolayers of bovine aortic endothelial cells primarily through low-affinity adsorptive endocytosis. The internalized PF-4 was degraded to amino acids and small peptides with 50% conversion after 18-h incubation. Thus, a secreted platelet protein can bind to and enter endothelial cells. Binding may explain the rapid clearance of released PF-4 from plasma and could have important local effects of endothelial structure and function.

L10 ANSWER 3 OF 7 COPYRIGHT 1993 ACS
TI Purification and characterization of heparinase from Flavobacterium heparinum
SO J. Biol. Chem., 260(3), 1849-57
AU Yang, Victor C.; Linhardt, Robert J.; Bernstein, Howard; Cooney, Charles L.; Langer, Robert
PY 1985
AN CA102(13):108647e
AB Heparinase (EC 4.2.2.7) isolated from F. heparinum was purified to homogeneity by a combination of hydroxylapatite chromatog., repeated gel filtration chromatog., and chromatofocusing. Homogeneity was established by the presence of a single band on both SDS- and acid-urea-gel electrophoretic systems. Amino acid anal. shows that the enzyme contains relatively high amts. of lysine residues (9%) consistent with its cationic nature (pI 8.5) but contains only 4 cysteine residues/polypeptide. The mol. wt. of heparinase was estd. to be 42,900 daltons by gel filtration and 42,700 daltons by SDS-polyacrylamide gel electrophoresis. The enzyme is very specific, acting only on heparin and heparan monosulfate out of 12 similar polysaccharide substrates tested. It has an activity max. at pH 6.5 and 0.1M NaCl and a stability max. at pH 7.0 and 0.15M NaCl. The Arrhenius activation energy was 6.3 kcal/mol. However, the enzyme is very sensitive to thermal denaturation and loses activity very rapidly at temps. >40.degree.. Kinetic studies of the heparinase reaction at 37.degree. gave a Km of 8.04 .times. 10-6M and a Vmax of 9.85 .times. 10-5 mol/min at a protein concn. of 0.5 .mu.g/mL. By adapting batch procedures of hydroxylapatite and QAE (quaternary aminoethyl)-Sephadex chromatog., gram quantities of heparinase that is nearly free of catalytic enzyme contaminants can be purified in 4-5 h.

L10 ANSWER 4 OF 7 COPYRIGHT 1993 ACS
TI An immobilized microbial heparinase for blood deheparinization
SO Appl. Biochem. Biotechnol., 9(1), 41-55
AU Linhardt, R. J.; Cooney, C. L.; Tapper, D.; Zannetos, C. A.; Larsen, A. K.; Langer, R.
PY 1984
AN CA101(4):28237k
AB A new medical application of an immobilized microbial enzyme is described. Heparinase [37290-85-0] isolated from Flavobacterium was immobilized and used in a fluidized bed reactor to eliminate heparin [9005-49-6] from blood passing through an extracorporeal circuit both in vitro and in vivo. The stepwise development of this heparinase reactor includes (1) improvements in the fermn. resulting in an inexpensive large-scale source of

heparinase without t[illegible] addn. of the previously [illegible]quired inducer, heparin; (2) the use of batch processes to adapt previous purifn. schemes to large-scale heparinase prodn. and the subsequent purifn. of heparinase to a single Na dodecyl sulfate-polyacrylamide gel electrophoresis banding protein; (3) the immobilization of heparinase with a 91% activity recovery and good stability, (4) the design and successful testing of a fluidized bed reactor contg. immobilized heparinase in the removal of clin. used quantities of heparin from both human blood in vitro and canine blood in vivo; and (5) the initiation of animal studies focusing on the toxicol. of heparinase-derived heparin degrdn. products and the short and long term effects of exposure to these products and to heparinase.

L10 ANSWER 5 OF 7 COPYRIGHT 1993 ACS
TI Heparinase
SO PCT Int. Appl., 9 pp.
AU Linhardt, Robert; Langer, Robert J.; Gallaher, Parrish M.; Cooney, Charles L.
PI WO 8200659 A1 4 Mar 1982
AI WO 81-US1081 12 Aug 1981
PY 1982
AN CA97(1):4688f
AB heparinase [9025-39-2] Is produced by fermn. with Flavobacterium heparinum on a chem. defined medium. Thus, F. heparinum ATCC 13125 was inoculated into a pH 7 broth contg. glucose 10, (NH4)2SO4 2, KH2PO4 2.5, NaH2PO4 2.5, MgSO4.7H2O 0.5, Na heparin 1, antifoam 0.1, histidine 0.5, methionine 0.5 g/L, and trace salts 10-4M and incubated at 23.degree. with stirring and aeration. After 25 h, the cells were harvested and sonicated, releasing 90% of the protein. The heparinase was purified by absorption and elution from hydroxyapatite [1306-06-5].

L10 ANSWER 6 OF 7 COPYRIGHT 1993 ACS
TI Involvement of cell surface heparin sulfate in the binding of lipoprotein lipase to cultured bovine endothelial cells
SO J. Clin. Invest., 68(4), 995-1002
AU Shimada, Kazuyuki; Gill, Peggy Jo; Silbert, Jeremiah E.; Douglas, William H.; Fanburg, Barry L.
PY 1981
AN CA95(23):201184y
AB The interaction of lipoprotein lipase (I), purified from bovine skim milk, with monolayer cultures of endothelial cells, isolated from bovine pulmonary artery, was evaluated. Endothelial cells in primary culture had no intrinsic I activity but were able to bind I quant. The binding reached equil. and was saturable at 0.24 nmol I/mg cell protein. The concn. of I at half-maximal binding was 0.52 .mu.M. Bound I could be detached from cultured cells by increasing concns. of heparin, and at .gtoreq.0.6 .mu.g/mL of heparin, 90% of the cell-bound I activity was released. Heparin sulfate and dermatan sulfate released I to a lesser extent and chondroitin sulfate caused little, if any, release of I. The release of I with heparin was not assocd. with a release of [35S]glycosaminoglycans from 35S-prelabeled cells. Redns. of I binding to endothelial cells and of cell surface-assocd. [35S]glycosaminoglycans in 35S-prelabeled cells occurred in parallel both when cells were pretreated with crude Flavobacterium heparinum enzyme before I binding and when cells were treated with this enzyme after I binding. The removal of heparan sulfate from the cell surface by purified heparinase totally inhibited the binding of I by endothelial cells, but the removal of chondroitin sulfate by chondroitin ABC lyase had no effect on this binding. These results

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      provide direct evidence for I attachment to endothelial cells
      through heparan sulfate on the cell surface and provide evidence for
      the release of I by heparin through a detachment from this binding
      site.

L10   ANSWER 7 OF 7  COPYRIGHT 1993 ACS
TI    Interaction of mucopolysaccharidases with glycosaminoglycans on
      glycosaminoglycan-bound AH-Sepharose 4B
SO    J. Biochem. (Tokyo), 84(4), 1005-8
AU    Ototani, Noboru; Yosizawa, Zensaku
PY    1978
AN    CA90(1):2201y
AB    Chondroitinase C, chondroitinase AC, heparinase, and heparitinase
      sepd. from an ext. of Flavobacterium heparinum were
      subjected to affinity chromatog. with glycosaminoglycan-bound
      AH-Sepharose 4B, previously coated noncovalently with
      glycosaminoglycan, as the matrix. The results suggest the importance
      of coating the matrix with glycosaminoglycan in the binding of the
      enzyme protein to the matrix.

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      FILE 'REGISTRY' ENTERED AT 15:50:55 ON 25 MAY 93
                E HEPARINASE II/CN 5
L1            2 S E2-E4
                E HEPARIN SULFATE/CN 5
L2            1 S E3
                E HYDROXYAPATITE/CN 5
L3            1 S E3
L4            0 S ALBUMIN/CN

      FILE 'CA' ENTERED AT 15:52:34 ON 25 MAY 93
L5        13440 S (L1 OR L2 OR L3 OR (HEPARINASE(W)(I OR II OR III))/IA)
L6            0 S L5 AND ((H OR HEPARINUM)(W)FAVOBACTERI?)/IA
L7            0 S L5 AND ((H OR HEPARINUM)(W)FLAVOBACTERI?)/IA
L8           91 S L5 AND FLAVOBACTER?/IA
L9           68 S L8 AND (L2 OR L3 OR (HEPARIN SULFATE OR HYDROXYAPATITE)
L10           7 S L9 AND (PROTEIN OR ALBUMIN)/IA

=> s l8 and (qae resin or cell lysate)/ia
            60 QAE/BI
           781 QAE/AB
           803 QAE/IA
                 (QAE/BI,AB)
        147607 RESIN/BI
        190786 RESIN/AB
        245044 RESIN/IA
                 (RESIN/BI,AB)
             1 QAE RESIN/IA
                 ((QAE(W)RESIN)/IA)
        386796 CELL/BI
        501847 CELL/AB
        680604 CELL/IA
                 (CELL/BI,AB)
          1013 LYSATE/BI
          4802 LYSATE/AB
          5161 LYSATE/IA
```

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               (LYSATE/BI,AB)
         667 CELL LYSATE/IA
               ((CELL(W)LYSATE)/IA)
L11            0 L8 AND (QAE RESIN OR CELL LYSATE)/IA

=> s 19 and (hplc or fplc)/ia
       30368 HPLC/BI
       53455 HPLC/AB
       61191 HPLC/IA
               (HPLC/BI,AB)
          73 FPLC/BI
         619 FPLC/AB
         638 FPLC/IA
               (FPLC/BI,AB)
L12            6 L9 AND (HPLC OR FPLC)/IA

=> s 112 not 110
L13            6 L12 NOT L10

=> d 1-6 .mh
```

L13 ANSWER 1 OF 6 COPYRIGHT 1993 ACS

TI Isolation and characterization of heparan sulfate proteoglycans produced by cloned rat microvascular endothelial cells

SO J. Biol. Chem., 267(7), 4859-69

AU Kojima, Tetsuhito; Leone, Cataldo W.; Marchildon, Gregory A.; Marcum, James A.; Rosenberg, Robert D.

PY 1992

AN CA116(19):189800p

AB Heparan sulfate proteolglycans (HSPGs) were isolated from cloned rat microvascular endothelial cells using a combination of ion-exchange chromatog., affinity fractionation with antithrombin III (AT III), and gel filtration in denaturing solvents. The anticoagulantly active heparan sulfate proteoglycans (HSPGact) which bind tightly to AT III bear mainly anticoagulantly active heparan sulfate (HSact) whereas the anticoagulantly inactive heparan sulfate proteoglycans (HSPGinact) possess mainly anticoagulantly inactive heparan sulfate (HSinact). HSact and HSinact were also isolated by a combination of ion-exchange chromatog., treatment with protease and chondroitin ABC lyase, and affinity fractionation with AT III. HSact and HSinact have mol. sizes of about 25-30 kDa with the same overall compn. of monosaccharides except that HSact exhibits about nine glucuronsyl 3-O-sulfated glucosamines/chain whereas HSinact possesses about three glucuronsyl 3-O-sulfated glucosamines/chain. Direct isolation of the AT III-binding site of HSact by exposing carbohydrate chains to <u>Flavobacterium</u> heparitinase in the presence of protease inhibitor revealed only a single interaction site which contained two to three glucuronsyl 3-O-sulfated glucosamine residues. The core proteins of HSPGact and HSPGin1ac1t were isolated by treatment with <u>Flavobacterum</u> heparitinase and purifn. by ion-exchange chromatog. The mol. sizes of the core proteins were established by SDS-PAGE and their primary structures were examd. by cleavage with trypsin or endopeptidase Glu-C as well as sepn. of peptides by reverse-phase <u>HPLC</u>. The results showed that both sets of core proteins exhibited three major components with mol. sizes of 50, 30, and 25 kDa, resp. The 25-kDa species appears to be a proteolytic degrdn. product of the 30-kDa species. The peptide mapping revealed that HSPGact and HSPGinact possess extremely similar core proteins.

L13 ANSWER 2 OF 6 COPYRIGHT 1993 ACS

TI <u>Heparinase</u> <u>II</u> from <u>Flavobacterium</u>

heparinum. HPLC analysis of the saccharides generated from chemically modified heparins

SO Eur. J. Biochem., 202(2), 531-41

AU Moffat, Colin F.; McLean, Maitland W.; Long, William F.; Williamson, Frank B.

PY 1991

AN CA116(9):79152w

AB Saccharides produced by the action of heparinase II on native pig mucosal heparin (heparin IS), de-N-sulfated heparin (heparin IH). N-Acetylheparin (heparin IA), de-N/O-sulfated heparin (heparin IVH), de-O-sulfated heparin (heparin IVS) and de-O-sulfated N-acetylheparin (heparin IVA) were analyzed by reversed-phase HPLC using Spherisorb ODS2. Fractions obtained by gel filtration with Bio-Gel P-4 were similarly examd. Heparin IS gave .DELTA.UA-2S .fwdarw. GlcNS-6S (IS) as the major unsatd. disaccharide and lesser amts. of .DELTA.UA .fwdarw. GlcNS-6S (IIS), .DELTA.UA-2S .fwdarw. GlcNS(IIIS), .DELTA.UA .fwdarw. GlcNS (IVS), .DELTA.UA-2S .fwdarw. GlcNAc-6S (IA), .DELTA.UA .fwdarw. GlcNAc-6S (IIA), .DELTA.UA-2S .fwdarw. GlcNAc (IIIA) and .DELTA.UA .fwdarw. GlcNAc (IVA). Heparins IA, IVA and IVS gave as the predominant unsatd. disaccharide that corresponding to the major repeat structure of the polymer. These were resp. .DELTA.UA-2S .fwdarw. GlcNAc-6S (IA), .DELTA.UA .fwdarw. GlcNAc (IVA) and .DELTA.UA .fwdarw. GlcNS (IVS). Minor disaccharides from the heterogeneous structure in native pig heparin and from residual O-sulfates after the de-O-sulfating process were detected. Heparin IH was degraded more slowly than any of the N-substituted heparins. The predominant unsatd. disaccharide was IH, which was derived from the major repeating unit. In addn., disaccharides IIH, IIIH, IA, IIA and IVA were detected. Heparin IVH showed little degrdn., the unsatd. disaccharide IVH not being detected after 24 h. Disaccharide IVA was obtained from the heterogeneous sequence in heparin IVH. Several higher oligosaccharides were identified in the gel-filtration fractions including saccharides from the linkage region (for heparin IS and IVA) and the anti-thrombin binding site (for heparin IS only). A tetrasaccharide and hexasaccharide, with the structures .DELTA.UA .fwdarw. GlcNAc .fwdarw. UA .fwdarw. GlcNAc and .DELTA.UA .fwdarw. GlcNAc .fwdarw. UA .fwdarw. GlcNAc .fwdarw. UA .fwdarw. GlcNAc, were present in the HPLC profiles of heparins IA and IVA.

L13 ANSWER 3 OF 6 COPYRIGHT 1993 ACS

TI Oligosaccharide mapping of low-molecular-weight heparins: structure and activity differences

SO J. Med. Chem., 33(6), 1639-45

AU Linhardt, Robert J.; Loganathan, Duraikkannu; Al-Hakim, Ali; Wang, Hui Ming; Walenga, Jeanine M.; Hoppensteadt, Debra; Fareed, Jawed

PY 1990

AN CA112(25):229301c

AB Low-mol.-wt. heparins from a variety of com. sources were examd. These had been prepd. by several methods, including peroxidative cleavage, nitrous acid cleavage, chem. .beta.-elimination, enzymic .beta.-elimination, and chromatog. fractionation. The mol. wts. and polydispersity of these low-mol.-wt. heparins showed greater differences than those of typical com. heparin prepns. Considerable differences were also obsd. in the antithrombin III-mediated anti-factor Xa activity, the heparin cofactor II-mediated anti-factor IIa activity, and the USP activity of these low-mol.-wt. heparins. An oligosaccharide-mapping technique (comparable to the peptide mapping of proteins) was applied to these heparins in an effort to understand the structural features responsible for their activity differences. Heparin lyase from Flavobacterium

heparinum was first used to depolymerize the low-mol.-wt. heparin into its constituent oligosaccharides. The oligosaccharides in the resultant mixt. were identified and quantitated by using std. oligosaccharides of defined structure in gradient polyacrylamide gel electrophoresis and strong-anion-exchange HPLC. Six of the oligosaccharide products were identified which represented nearly 90% of the heparin mass. Even though all the low-mol.-wt. heparins showed these 6 oligosaccharide components, their content in each varied greatly, accounting for 20 to >90% of their mass. The antithrombin III-mediated anti-factor Xa activities of the low-mol.-wt. heparins correlated only poorly with the concn. of a hexasaccharide contg. a portion of heparin's antithrombin III-binding site. The heparin cofactor II-mediated anti-factor IIa activity, however, could not be correlated with these 6 oligosaccharides of known structure nor with the mol. wt. or charge d. of these low-mol.-wt. heparins. The low-mol.-wt. heparins prepd. by different methods each showed a new distinctive oligosaccharide in their maps. Their isolation and structural characterization, which included 2-dimensional NMR and fast atom bombardment mass spectrometry, indicated that these unusual oligosaccharides result from end-sugar modification during chem. depolymn. Both gel electrophoresis and HPLC mapping techniques showed a greater structural diversity between low-mol.-wt. heparins than had previously been obsd. between similarly analyzed com. heparins.

L13 ANSWER 4 OF 6 COPYRIGHT 1993 ACS
TI Examination of the substrate specificity of heparin and heparan sulfate lyases
SO Biochemistry, 29(10), 2611-17
AU Linhardt, R. J.; Turnbull, J. E.; Wang, H. M.; Loganathan, D.; Gallagher, J. T.
PY 1990
AN CA112(13):114696t
AB The activities of different prepns. of heparin and heparan sulfate lyases from Flavobacterium heparinum were examd. The enzymes were incubated with oligosaccharides of known size and sequence and with complex polysaccharide substrates, and the resulting degrdn. products were analyzed by strong-anion-exchange HPLC and by oligosaccharide mapping using gradient PAGE. Heparinase (EC 4.2.2.7) purified in this lab. and a so-called Heparinase I (Hep I) from a com. source yielded similar oligosaccharide maps with heparin substrates and displayed specificity for di- or trisulfated disaccharides of the structure .fwdarw.4)-.alpha.-D-GlcNp2S(6R)(1 .fwdarw. 4)-.alpha.-L-IdoAp2S(1 .fwdarw. (where R = O-sulfo or OH). Oligosaccharide mapping with 2 different com. prepns. of heparan sulfate lyase [heparitinase (EC 4.2.2.8) and Heparinase III (Hep III)] indicated close similarities in their depolymn. of heparan sulfate. Furthermore, these enzymes only degraded defined oligosaccharides at hexosaminidic linkages with glucuronic acid: .fwdarw.4)-.alpha.-D-GlcNpR(1 .fwdarw. 4)-.beta.-D-GlcAp(1 .fwdarw. (where R = N-acetamido or N-sulfo). The enzymes showed activity against solitary glucuronate-contg. disaccharides in otherwise highly sulfated domains including the saccharide sequence that contains the antithrombin-binding region in heparin. A different com. enzyme, Heparinase II (Hep II), displayed a broad spectrum of activity against polysaccharide and oligosaccharide substrates, but mapping data indicated that it was a sep. enzyme rather than a mixt. of heparinase and heparitinase/Hep III. When used in conjunction with the described sepn. procedures, these enzymes are powerful reagents for the structural/sequence anal. of heparin and heparan sulfate.

L13 ANSWER 5 OF 6 COPYRIGHT 1993 ACS
TI Homogeneous, structurally defined heparin-oligosaccharides with low anticoagulant activity inhibit the generation of the amplification pathway C3 convertase in vitro
SO J. Biol. Chem., 263(26), 13090-6
AU Linhardt, Robert J.; Rice, Kevin G.; Kim, Yeong S.; Engelken, John D.; Weiler, John M.
PY 1988
AN CA109(17):142049r
AB Heparin-oligosaccharides were prepd. by partial depolymn. of heparin by using purified flavobacterial heparinase. The resulting oligosaccharide mixt. was then fractionated by using strong anion exchange-HPLC to produce individual oligosaccharide components of this mixt., with degree of polymn. ranging 2-16. These heparin-oligosaccharides were examd. for both their anticoagulant activity and capacity to inhibit activation of the amplification pathway of complement. Although there was little difference among com. heparins, a correlation between mol. wt. and activity to inhibit convertase generation was clearly established for heparin-oligosaccharides between d.p. 2 through 16. Heparin-oligosaccharides of degree of polymn. 10-16 (Mr 3888-5320) demonstrated up to 54% of heparin's activity on a molar basis (and up to 163% of heparin's activity on a wt. basis) in inhibiting the amplification pathway of complement in vitro while showing almost no anticoagulant activity. Thus heparin-oligosaccharides with low anticoagulant activity have a high capacity to inhibit activation of the amplification pathway of complement in vitro. These studies, for the 1st time, completely sep. heparin's ability to inhibit complement activation from its anticoagulant activity.

L13 ANSWER 6 OF 6 COPYRIGHT 1993 ACS
TI Fractionation of heparin-derived oligosaccharides by gradient polyacrylamide-gel electrophoresis
SO Biochem. J., 244(3), 515-22
AU Rice, Kevin G.; Rottink, Mary K.; Linhardt, Robert J.
PY 1987
AN CA107(3):20255t
AB Heparin-derived oligosaccharides, prepd. by using flavobacterial heparinase, having a high degree heterogeneity (sequence variability) were resolved into sharp well-defined bands by using PAGE. The use of a stacking gel and a high-d.-pore-gradient resolving gel was primarily responsible for the success of this sepn. Low-mol. wt. stds. of known structure and having a a d.p. 2-6 were used to establish that the sepn. on gradient PAGE was primarily dependent on mol. size. High-mol.-wt. oligosaccharides (d.p. 8-20) were prepd. using strong-anion-exchange HPLC and were used to help characterize the gradient PAGE sepn. Kinetic profiles were obtained for the depolymn. of heparin and heparan sulfate with heparinase and heparitinase, resp. The utility of this approach in sequencing oligosaccharides derived from glycosaminoglycans is discussed.

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=> s 18 and (monoclonal antibod? or mouse myeloma)/ia
      24763 MONOCLONAL/BI
      43454 MONOCLONAL/AB
      47187 MONOCLONAL/IA
              (MONOCLONAL/BI,AB)
      74992 ANTIBOD?/BI
     135775 ANTIBOD?/AB
     150169 ANTIBOD?/IA
              (ANTIBOD?/BI,AB)
```

41222 MONOCLONAL ANTIBOD?/IA
((MONOCLONAL(W)ANTIBOD?)/IA)
62699 MOUSE/BI
97653 MOUSE/AB
122307 MOUSE/IA
(MOUSE/BI,AB)
3738 MYELOMA/BI
6174 MYELOMA/AB
7624 MYELOMA/IA
(MYELOMA/BI,AB)
1854 MOUSE MYELOMA/IA
((MOUSE(W)MYELOMA)/IA)
L14 1 L8 AND (MONOCLONAL ANTIBOD? OR MOUSE MYELOMA)/IA

=> d .mh

L14 ANSWER 1 OF 1 COPYRIGHT 1993 ACS
TI The mechanism of precartilage mesenchymal condensation: a major role for interaction of the cell surface with the amino-terminal heparin-binding domain of fibronectin
SO Dev. Biol., 136(1), 97-103
AU Frenz, Dorothy A.; Jaikaria, Navdeep S.; Newman, Stuart A.
PY 1989
AN CA111(21):192109x
AB Using low-magnification Hoffman Modulation Contrast microscopy to rapidly identify precartilage mesenchymal condensations in chick limb bud cultures, the effect was detd. on condensation no. of treatments disruptive of the interaction of cell surface components with endogenously produced fibronectin. A monoclonal antibody directed against the N-terminal heparin-binding domain of fibronectin reduced the no. of condensations by >50%, as did the oligopeptide Gly-Arg-Gly, which is a repeated motif in that fibronectin domain. In contrast, monoclonal antibodies directed against the collagen- and integrin-binding domains of fibronectin, or oligopeptides contg. the fibronectin integrin-recognition sequence Arg-Gly-Asp-Ser, had no significant effect on condensation no. Addn. of Flavobacterium heparinase to cultures also reduced condensation no. by >50%. Alcian blue staining of sulfated proteoglycan was greatly reduced in differentiated cultures that had been exposed to treatments that reduced condensation no. Taken together with the accompanying study, which directly demonstrates an adhesive interaction between the N-terminal domain of extracellular fibronectin and heparin-like mols. on the surfaces of latex bead probes, the data presented here strongly indicate a major role for the corresponding cell-matrix interaction in mediating precartilage condensation in limb mesenchyme.

=> fil .biotech
FILE 'BIOSIS' ENTERED AT 16:06:52 ON 25 MAY 93

FILE 'MEDLINE' ENTERED AT 16:06:52 ON 25 MAY 93

FILE 'EMBASE' ENTERED AT 16:06:52 ON 25 MAY 93

=> s heparinase(w)(i or ii or iii) and (h or heparinum)(W)flavobacteri?
FILE 'BIOSIS'
420 HEPARINASE